EDITORIAL

When a Measure is Consequential

Cuando una medida es primordial

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"When you can measure what you are speaking about, and express it in numbers, you know something about it, when you cannot express it in numbers, your knowledge is of a meager and unsatisfactory kind"
William Thomson, 1st Baron Kelvin

"If you can't measure it, you can't improve it."
Peter Drucker

Defining cardiotoxicity always has significant clinical implications and yet there is no standard, widely accepted, nor clinical outcomes-linked definition for this entity. Over the years, there has been a variety of efforts to try to find a reasonable and objective way to make a valid and reliable diagnosis of cardiotoxicity that is undoubtedly related to the anticancer treatment in question. As it stands in our current practice, the most accepted methods still depend on following, certainly costly, but objective cardiac tests to make this diagnosis.

As the authors of this manuscript well elaborate (1), monitoring during treatment of breast cancer with serial echocardiography is the most widely accepted regimen in America and likely worldwide.

Data from sizeable adjuvant trastuzumab trials suggest that the proportion of patients who suffer asymptomatic left ventricular ejection fraction (LVEF) declines during or after trastuzumab therapy in curative-intent treatment groups ranges from 4% to 30%, but rates of symptomatic congestive heart failure (CHF) are much lower (0.6% to 3.8%). (2-6) Also, despite considerable efforts to discover the true molecular and mechanistic aspects of trastuzumab-induced cardiotoxicity, the potential causative process remains incompletely understood. Trastuzumab-induced cardiac dysfunction is regarded as less severe and largely reversible because primary cardiomyocyte injury has not occurred in patients treated with trastuzumab in biopsy studies. Indeed, this agent has not shown the same ultrastructure changes traditionally described with anthracycline-induced cardiotoxicity.

It is also useful baseline to understand that the risk factors that appear to be associated with a higher likelihood of developing trastuzumab-related cardiotoxicity include age (seemingly greater than 50), previous or concurrent anthracycline use, and particularly patients above normal weight. (7-13) This is important to notice since the current group reports patients slightly above this age and with a considerable degree of obesity.

As we can extrapolate from the variety of clinical trials looking at hard outcomes and mortality based on declined left ventricular ejection fraction (14), this measure, the final number on our echocardiogram report is indeed a compelling value. Given the nature and mechanism with trastuzumab, we may be very well dealing with a new process, where a transient LVEF decline, which is what is noted in the vast majority of patients, and was also the case of this study, still does not have the same long-term prognostic weight that we have been used to in the past. This would be, however, much-welcomed information for patients dealing with the type of cancers where trastuzumab is essential therapy.

This study also serves to point out that the choice of methodology for our follow-up in cardiac monitoring is essential. We must exert a balance of judgment when using any particular criteria. It is interesting to see in this report that one criteria would find significant LVEF drop in the neighborhood of 60% incidence. No previous trial has described this degree of incidence, and it would be important to know if there is any explanation related to ethnicity in this exclusively Latin population or if there are unique genetic predispositions in Hispanics. In this regard, racial differences have been described in the literature. There is at least one recent report where a disproportionate distribution of cardiotoxicity in patients of color was documented. (15)

However, most importantly is that our quality in imaging meets a certain standard. Meaning, what good is to follow a drop of ten points in LVEF if our intra-observer variability is 20%? Therefore, we should

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always use the most advanced quantification method available to us for LVEF measurements and become proficient and achieve expert hands at this, before using the measures to make clinical decisions or sharing serious pieces of information with our patients.

Conflicts of interest

None declared.

(See authors' conflicts of interest forms on the website/Supplementary material).

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